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LOCAL ANTIBIOTICS IN SKIN INFECTIONS.

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In recent years, the local treatment of infective diseases of the skin has centred to a great extent on the use of a suitable antibiotic. The choice was formerly strictly limited and therefore relatively simple. The advent of a larger number of antibiotics and the development of antibiotic resistance has gradually made this choice much more complicated.

Laboratory sensitivity tests assist considerably in the selection of an appropriate drug. This help is not always available : even where it is, there is an inevitable delay before the report on the tests is received. Consequently where antibiotic therapy is to be initiated immediately it must always be commenced " blind ", that is, before sensitivities have been assessed or without such assessments at all.

In such circumstances, treatment can only be rational if the clinician is aware of which organism is likely to be responsible and if he also knows the current state of antibiotic resistance. Since, in dermatology, the bacteria usually associated with infections are well known and fairly constant, it is often possible to suppose which organism is to be tackled. Antibiotic resistance is inconstant and its current state or trends at any one time can be gauged only by reference to recent assessments.

This paper records the incidence of infecting organisms in two groups of infections encountered in a city out-patient dermatological department in the years 1954 and 1957 ; the antibiotic sensitivity of the organisms has been assessed and comparisons made between these groups.

Investigations.

Two series of cases have been examined. The first concerns an outbreak of impetigo, mostly bullous, occurring during the latter half of 1954. The second

deals with a group of miscellaneous skin infections seen throughout the year 1957. Certain aspects of these series are outlined below.

The organisms associated with the cases of impetigo have been reviewed and their incidence entered in Table I. A pyogenic *Staphylococcus aureus* was present in 97·5% of cases and a beta-haemolytic streptococcus in 18·75% of cases. The organisms concerned in the 1957 group have been similarly analysed and the results recorded in Table II. Here, a pyogenic *Staphylococcus aureus* was present in no less than 92·49% of cases, a beta-haemolytic streptococcus in 23·11% of cases, and a Gram negative organism in 11·32% of cases (*B. proteus*, *Ps. pyocyaneus* or coliform bacilli).

TABLE I.—*Bacteriological Analysis of Impetigo Series*, 1954.

80 cases.

Organisms.	Cases %.
Staphylococcus aureus only	81·25
Beta-haemolytic streptococcus only	2·50
Staphylococcus and streptococcus mixed	16·25
Total	100·00
Staphylococcus aureus (pure and mixed culture)	97·50
Beta-haemolytic streptococcus (pure and mixed culture)	18·75

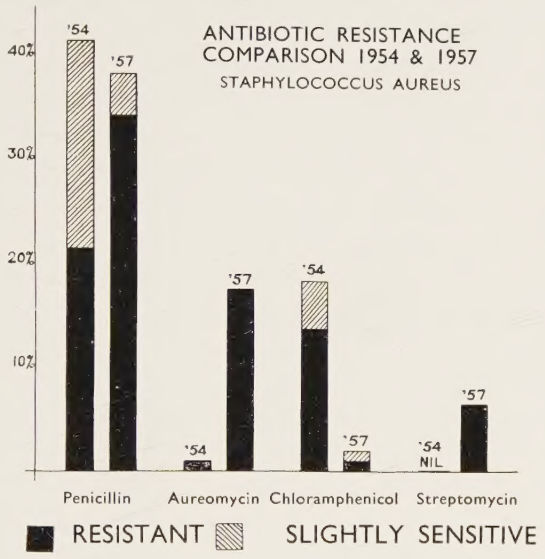
TABLE II.—*Bacteriological Analysis of Miscellaneous Infections*, 1957.

212 cases.

Organisms.	Cases %.
Staphylococcus aureus only	68·44
Beta-haemolytic streptococcus only	2·36
Staphylococcus and streptococcus mixed	17·92
Single Gram negative organism only	2·36
Mixed Gram negative organisms	0·94
Gram negative organism and staphylococcus mixed	5·15
Gram negative organism and streptococcus mixed	1·89
Gram negative organism and staphylococcus and streptococcus mixed	0·94
Total	100·00
Staphylococcus present (pure and mixed culture)	92·49
Streptococcus present (pure and mixed culture)	23·11
Gram negative organism present (pure and mixed culture)	11·32

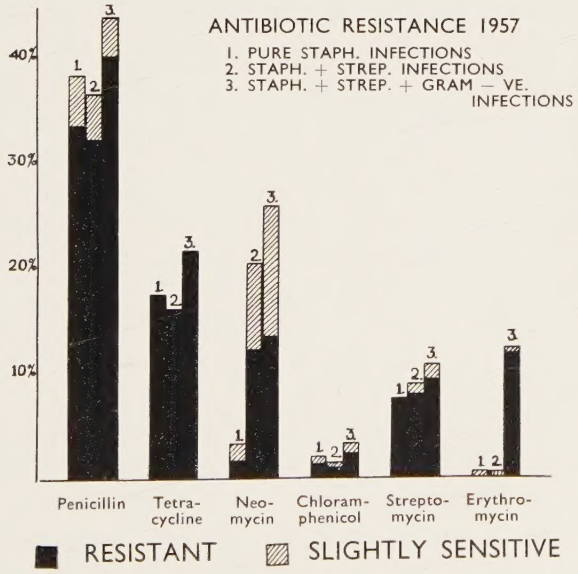
Sensitivities of the various organisms in the 1954 series were assessed to penicillin, chlortetracycline, chloramphenicol and streptomycin and in the 1957 series to these and also to tetracycline, neomycin and erythromycin. It has thus been possible to compare the sensitivities to the four former antibiotics in the respective series. The comparison of pure staphylococcus infections is recorded graphically in Fig. 1. This shows an increase in resistance to penicillin from 21·5% to 34·3% and to chlortetracycline from 1·0% to 16·0% and a decrease in resistance to chloramphenicol from 13·7% to 1·0%. The emergence of some resistance to streptomycin (nil to 6·5%) is also shown. This antibiotic

will not be discussed further since it is not usually employed locally in treating skin infections because of the high risk of contact dermatitis.



SENSITIVITIES ASSESSED IN 65 CULTURES, 1954.
IN 197 CULTURES, 1957 (TO AUREOMYCIN IN 148 CULTURES, 1957)

Fig. 1.



SENSITIVITIES ASSESSED IN 212 CASES (TO NEOMYCIN IN 163 CASES)

Fig. 2.

The picture of antibiotic resistance for the entire 1957 series is recorded in Fig. 2. The intention is to reflect the likely efficacy of the various antibiotics in infections caused by the groups of organisms commonly encountered in skin infections. Tetracycline has been substituted for chlortetracycline since there were more sensitivity reports available with the former. Cross resistance among the tetracyclines has been widely accepted. Although there have been reports of inconsistency of cross resistance to these drugs (Culbertson, 1957 ; Jen-Yah Hsie, 1957), the author found only one such inconsistency when he compared tetracycline and chlortetracycline in a significant number of cases. (The data on erythromycin have been recorded for interest only, since it is not proposed to advocate the use of this antibiotic in the local treatment of skin infections. Sensitivities were assessed by the disc method.

The problem of antibiotic resistance is largely one of staphylococcal resistance. This is certainly true in dermatology for staphylococci predominate in skin infections. Bigger and Hodgson (1943) reported staphylococal growths in 97% of cultures from impetigo lesions. In the impetigo series recorded here, staphylococci were present in 97·5% of cases. Davies *et al.* (1945) encountered staphylococci in 96·5% of cultures from a group of miscellaneous skin infections. The miscellaneous group reported here yielded staphylococci in 92·49% of cases, a figure which would have been higher had infections associated with Gram negative bacilli been excluded as in the group of Davies *et al.* It is clear, therefore, that effectiveness against the staphylococcus is an essential requirement of an antibiotic that is to be used in treating the general run of skin infections ; conversely, the development by staphylococci of resistance to an antibiotic seriously diminishes the usefulness of that antibiotic in dermatology.

Staphylococci and Penicillin.

Such a diminution in general efficacy has already been observed with penicillin. Staphylococcal resistance to penicillin has gradually increased in those areas of the world where it has been used widely. In general, resistance has been higher where cultures have been made from hospital in-patients, lower where they have been made from hospital out-patients and still lower where they have been obtained from sources beyond the hospital environment (Finland, 1955). For example, Fusillo *et al.* (1954) found a resistance rate of 80·5% among in-patients, 32·4% among out-patients and only 6·7% in a community. Their figure for out-patients represents an increase in resistance when the assessments of 6·7% (Griffiths *et al.*, 1949) and 16·0% (Birnstingl *et al.*, 1952) are compared. Although Shooter (1954) has pointed out that resistant staphylococci may be as common in dermatological and ear, nose and throat out-patient departments as within hospitals, I have found resistance to be lower among out-patients compared with in-patients. Nevertheless, the assessment of 70% resistance among " city " patients in Paris (Terrial and Chabbert,

1955) indicates the extent to which resistance can develop with the in-patient groups. The exact degree of penicillin resistance may vary from place to place. The important point is that penicillin resistance is increasing among out-patients and probably in the community at large to such an extent that the blind use of penicillin is likely to be followed, either now or in the near future, by failure to cure infection in an unacceptably large proportion of cases. The usefulness of penicillin, therefore, in the treatment of skin infections in particular appears to be coming to an end, except, perhaps where pure streptococcal infections are concerned.

Staphylococci and the Tetracyclines.

Similar trends have been observed in the relationship between staphylococci and the tetracyclines. Fusillo *et al.* (1954) have reported a resistance rate of 71·5% among in-patients, 17·6% among out-patients and 3·8% in a community. Fairbrother *et al.* (1951) could report a resistance rate of only 0·5% in staphylococci isolated from routine hospital material. This indicates a marked increase in resistance on the part of staphylococci to the tetracyclines. My figures illustrate this increase in relation to out-patient sources. Unless this trend is arrested, the tetracyclines, hitherto so useful in treating skin infections, seem likely to meet the same fate as penicillin, with again the exception of pure streptococcal infections. The future of this group of antibiotics in dermatology is thus doubtful.

Staphylococci and Neomycin.

In regard to neomycin, Waisbren (1956) states that staphylococcal resistance is rare. This is supported by Rantz and Rantz (1956) who found resistance in only 1·2% of cases. In the 1957 series reported here, resistance in only 1·3% of cases correlates closely with this. Doniger and Parenteau (1957), however, have reported decreasing effectiveness of neomycin against staphylococci. One wonders if this is an indication that a more widespread and increasing resistance to neomycin may develop although it is never used systemically. Nevertheless at present neomycin still appears on the whole to be an effective antibiotic against the staphylococcus.

Staphylococci and Chloramphenicol.

Chloramphenicol has retained its strength against the staphylococcus strikingly well. Culbertson (1957) has shown that most strains of staphylococci were consistently sensitive throughout a five year period to 1956. Although he presents his survey in graphic form, it appears that the sensitivities have been well above 90% throughout ; the greatest resistance was about 10% in the first quarter of 1952. In the 1954 series of the present report 13·7% were

resistant, which is very close to the figures of Clapper *et al.* (1954) who found 12·0% resistant. Rantz and Rantz (1956) recorded the lower finding of 5·8% and my 1957 series gave only 1·0% resistant. Thus, although a little resistance to chloramphenicol has been recorded, the trend at present seems to be towards increasing sensitivity.

I am indebted to Dr. Margaret Little, Skin Department, Victoria Infirmary, Glasgow, for information relating to a group of miscellaneous skin infections occurring between April and August, 1958, among out-patients. In 92 cases where a pyogenic *Staphylococcus aureus* was cultured the following resistance rates were encountered :—

	%
Penicillin	61·0
Tetracycline	17·3
Chloramphenicol	3·2
Neomycin	2·0
Streptomycin	5·4
Erythromycin	0·5

There is reflected a marked increase in resistance to penicillin compared with the figures for 1957, very slight and possibly insignificant increases in resistance to tetracycline, chloramphenicol and neomycin and a very slight and possibly insignificant decrease in resistance to streptomycin. Resistance to erythromycin is unchanged.

Mixed Staphylococcal and Streptococcal Infections.

Of the antibiotics reviewed here, chloramphenicol and neomycin appear almost equally effective against the staphylococcus. In assessing when and how to use these drugs, however, attention to certain additional factors is required. Although a staphylococcus is present in over 90% of skin infections, it is present alone less frequently. Davies *et al.* (1954) found only 51% of lesions gave a pure culture, the remainder being mostly mixed staphylococcal and streptococcal infections. In the 1957 series presented here, 68·44% of infections were purely staphylococcal and in the remaining infections an appreciable number of streptococcal cultures was obtained (Table II). Therefore, with regard to " blind " therapy, allowance must be made for the presence of a streptococcus in a significant proportion of cases. The frequent inability of neomycin to cope with streptococcal infections may thus suggest that chloramphenicol is the better choice of remedy, but the solution is not so simple. With the development of so much resistance to penicillin and the tetracyclines, it may be argued that chloramphenicol should be reserved for systemic use in serious or potentially serious infections due to organisms resistant to other antibiotics. Moreover, chloramphenicol may produce severe epidermal sensitization. Neomycin seems less prone to produce such reactions and is thus safer to use locally. Attention has recently been focused on skin sensitivity to

neomycin (Calnan and Sarkany, 1958). The increase in sensitivity they report underlines the need for reserve in prescribing this antibiotic. Nevertheless, it is still the author's experience that neomycin is less prone to produce sensitization than chloramphenicol. Its weakness against the streptococcus has been partially met by the production of ointments or creams, combining it with either bacitracin or gramicidin. While these preparations are undoubtedly useful, intolerance to their vehicle may develop following application in the more acute phases of skin infections.

Pure Streptococcal Infections.

Pure streptococcal infections do not constitute a major problem in dermatology. They are uncommon : Davies *et al.* (1954) recorded only 3·0% of their cultures as purely streptococcal and Bigger and Hodgson (1943) found only 2·0% of impetigo cases were due to the streptococcus alone. In the present investigation only 2·5% of impetigo cases in 1954 and 2·36% of miscellaneous infections in 1957 were purely streptococcal. Further, relatively little streptococcal resistance to antibiotics has been reported (Terrial and Chabbert, 1955 ; Lepper, 1955). Resistance to neomycin is a noteworthy exception, but this is to a great extent a natural resistance.

Gram Negative Bacillary Infections.

In dermatological practice pure Gram negative bacilli offer the most resistance after staphylococci. Although pure Gram negative infections are uncommon, constituting only 2·36% in the 1957 group recorded here, the culture of such organisms in pure or mixed growths in 11·32% of cases in the same group suggests that they must not be overlooked. In the above group, these organisms were usually found in relatively chronic conditions such as varicose ulceration or otitis externa. Their presence may constitute an important cause of delayed healing. Analysis of this group, admittedly small, has suggested that penicillin is completely ineffective against the Gram negative bacilli, and tetracycline is almost completely ineffective against *B. proteus* and *Ps. pyocyaneus*, but commonly effective against coliform bacilli. Neomycin is quite variable in its action against all three and chloramphenicol is consistently effective against *B. proteus* and coliform bacilli and effective more often than not against *Ps. pyocyaneus*. In " blind " application, therefore, chloramphenicol is much more likely to cure Gram negative infections than any of the other drugs discussed. (Gentian violet not uncommonly clears such infections without recourse to antibiotics.)

Sensitivity Tests.

Where an organism is found to be sensitive to an antibiotic *in vitro*, satisfactory clinical response in my experience invariably follows. This may not be

a universal finding. In assessing clinical response with regard to sensitivity tests, it must be remembered that the apparent failure of an antibiotic preparation to cure an infection is not necessarily clinical evidence of insensitivity of the organism or an indication of an inaccurate laboratory report. Such failure may be due to the nature of the vehicle. The close correlation already mentioned between *in vitro* sensitivities and clinical results may be due to the deliberate use in this Department of aqueous solutions of antibiotics. The application of antibiotics in ointment or cream bases may be associated with certain disadvantages. Florestano *et al.* (1956) have shown that there is a considerable difference in the rate of liberation of antibiotics from greasy and non-greasy ointment bases. For example, in a laboratory investigation closely simulating *in vivo* conditions, a preparation containing 0·75 mg. of neomycin per gram of water miscible base was just as effective as, if not more effective than, another preparation containing 5·0 mg. of neomycin per gram of greasy petrolatum base. One wonders whether preparations in a greasy base may on occasion fail to act through inadequate liberation of antibiotic. Even if this is not so, it must be agreed that the employment of such greasy bases demands the use of an extravagant quantity of the active principle.

Intolerance to the base may develop due to the physical character of the vehicle by preventing evaporation or escape of fluid or radiation of heat from the lesion ; as one would expect, this is encountered mainly in oozing or hot oedematous phases. It is distinct from true hypersensitivity ; healing is merely retarded and patch tests negative. We have frequently encountered in this Department cases of acute bullous impetigo which failed to respond to an antibiotic in an ointment or cream base, even where the organism was sensitive ; administration of the same antibiotic in aqueous solution resulted in rapid loss of oedema and oozing to such an extent that greasy preparations were well tolerated immediately thereafter. Base intolerance may explain the comment of Kile *et al.* (1952) who, in treating various types of skin infections with neomycin in several different vehicles, found that " the ointments caused irritation in several patients on whom patch tests were negative ". These workers found such reactions difficult to interpret.

The use of aqueous solutions of antibiotics introduces the disadvantage of the general instability of antibiotics in water. This problem may be overcome in the instances of penicillin and the tetracyclines, by prescribing solution tablets outside hospital and by preparing and frequently renewing small quantities of appropriate solutions within the hospital. Aqueous solutions of chloramphenicol can be rendered stable for about a month by incorporating a borax-boric acid buffer : chloramphenicol 0·5%, borax 0·3%, boric acid 1·5%, water q.s.* Neomycin is an exception : for almost all practical purposes it is stable indefinitely in water. Aqueous solutions of neomycin in a strength of 0·1%,

* I am indebted to Messrs. Parke, Davis & Co., Ltd. for this formula.

usually applied by spraying or dabbing, have been used most effectively in this Department when the organism was sensitive. Aqueous solutions of chloramphenicol 0·5% and aureomycin 0·5% have likewise been effective. The use of antibiotics in this way has many advantages. The antibiotic is not held back by its vehicle and makes contact with the lesion immediately. Base intolerance does not develop and thus healing is not delayed. If improvement does not occur, it is almost certainly because the organism is insensitive, provided solutions of adequate strength have been used. Moreover, aqueous solutions are cheaper, which is important. Should true sensitivity to any constituent of a preparation develop, it is more likely to be worse when an ointment or cream is employed.

Of the various antibiotics discussed here, chloramphenicol has emerged as the antibiotic most likely to cure most skin infections whatever the causative organism. This highly favourable position of chloramphenicol may be related to its relatively small use in the past. One wonders if this fortunate state will continue ; whether, if the development of each new antibiotic is followed by a steadily overtaking trail of resistance and even skin intolerance, the usefulness of antibiotics will one day be lost. The supply of adequate new antibiotics may not be inexhaustible ; even if it were, it is unlikely that the development of each new drug would be other than expensive. The intensive employment of antibiotics has too frequently been followed by the development of resistance ; subsequent restriction of use has re-established sensitivity. Where antibiotics have not been used intensively, low resistance rates have usually been encountered. The implications seem obvious but the recurrent pleas for greater reserve in prescribing antibiotics suggest that the warnings are still frequently unheeded. In dermatology, infections seldom endanger life ; indeed, they are often quite trivial. There is thus great scope for restricting the use of antibiotics in this field and contributing either to the lowering of resistance or to the prevention of further increases. The methods of the pre-antibiotic age were often quite adequate in the treatment of skin infections. In this Department considerable benefit has been obtained for many years from the use of gentian violet, usually in extremely weak solutions scarcely staining the skin at all (1 in 30,000). In the less common presence of secondary infection with Gram negative organisms, stronger concentrations which stain may be necessary. Other preparations, such as ichthyol, can likewise benefit skin infections and employment of them spares the use of antibiotics.

Summary.

The staphylococcus retains its position as the organism causing most skin infections. Pure streptococcal and pure Gram negative bacillary infections are uncommon. The possibility of a streptococcus or a Gram negative organism

being present in a mixed infection, however, cannot be ignored, especially in the case of the streptococcus.

Data are presented to show that resistance on the part of the staphylococcus to penicillin and the tetracyclines is steadily increasing among out-patients. Chloramphenicol is maintaining its effectiveness against this organism.

Pure streptococcal infections do not constitute a major problem in dermatological practice. The streptococcus is usually sensitive to the major antibiotics but resistance to neomycin is common.

Chloramphenicol is effective in Gram negative bacillary infections more often than the other antibiotics discussed, viz. penicillin, the tetracyclines and neomycin.

Chloramphenicol has emerged as the antibiotic most likely, on the basis of sensitivity reports, to cure most skin infections.

Clinical response usually correlates closely to the sensitivity reports. This may be due to the use of antibiotics in aqueous solutions during the more acute phases of infections. The use of antibiotics in this way is discussed, together with the question of base intolerance.

The present position of antibiotics in relation to skin infections is reviewed. It is strongly suggested that the use of such agents should be restricted as much as possible and non-antibiotic remedies employed.

I wish to acknowledge the kind help and criticism of Dr. Mary Sloan Smith in the preparation of this paper. I also wish to thank the Bacteriology Staff of the Glasgow Victoria Hospitals Group for providing the reports on sensitivities.

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COMPARISON OF TOPICAL STEROIDS.

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The safety and usefulness of steroid applications in the treatment of eczema is beyond dispute. The relative efficacy of the available preparations is less certain.

Frank and Stritzler (1955) compared $\frac{1}{4}\%$ and $\frac{1}{2}\%$ prednisolone ointment with 1% hydrocortisone ointment in a large number of dermatoses. They found the 1% hydrocortisone ointment more effective. Surprisingly, increasing the concentration of prednisolone from $\frac{1}{4}$ to $\frac{1}{2}\%$ did not increase its effectiveness. They do not seem to have made a controlled trial on in-patients.

Conrad Smith (1956) compared the response of 40 patients with itching skin dermatoses and found 1% hydrocortisone ointment more effective than $\frac{1}{2}\%$ prednisolone ointment. His cases, however, do not appear to have been in-patients where regular and accurate dressings were applied by trained nurses.

Frolow, Witten and Sulzberger (1957) found that "neither prednisolone nor prednisone was more effective than double its concentration of hydrocortisone" for local use. However, the method of leaving each patient to "rub small amounts of the test ointments into the designated areas of the skin 2 or 3 times daily, and to take care to avoid contamination of other sites" would seem to be a crude.

On the other hand, Zimmerman (1956) found that "prednisolone alcohol when used in only one half the concentration of hydrocortisone free alcohol is as effective as or slightly more effective than the latter in the topical therapy of various dermatoses". His patients were observed only at "approximately weekly intervals", the applications being self-used and apparently without occlusive dressings.

Peter Borrie (1958), however, treated 30 in-patients with various itching skin conditions, comparing $\frac{1}{4}\%$ prednisolone ointment with 1% hydrocortisone ointment on alternate patients and found the applications equally effective.

Because of these conflicting reports it was decided to test a brand of 1% hydrocortisone ointment in general use in this Skin Service against $\frac{1}{4}\%$ prednisolone ointment. The 1% hydrocortisone ointment contained the acetate in a proprietary greasy base. The $\frac{1}{4}\%$ prednisolone ointment contained the free alcohol in a water miscible base, described as a mixture of glycols, with 15% soft paraffin in hydrophilic form. The manufacturers state that they changed their local steroid preparations two years ago from acetate to free alcohol for convenience of manufacture.

Method.

In order that the results could be assessed with the greatest possible accuracy, it was decided to perform the trial on the first 25 cases presenting in this clinic with the following characteristics.

(i) The cases had to be severe enough to be treated as in-patients. This meant that the dressings were done skilfully and accurately and observed each day, the sister in charge making detailed daily notes of progress.

(ii) Only cases showing symmetrical eczema of the limbs were accepted for the trial. Moreover, not only were the cases symmetrical, but of approximately equal severity on each side.

The $\frac{1}{4}\%$ prednisolone ointment was always applied to the right limb and the 1% hydrocortisone ointment always to the left. In the wards these preparations were called respectively P2 and F2. Since it took nearly four months to gather the 25 cases to be tested, there were only a few on the trial in the wards at the same time and they were therefore not easily able to compare notes and influence each other. The minimum period of observation on the trial was ten days, with one exception. The dressings were accurately performed thrice daily with "Tubegauz", each application being gently laid on top of the previous one without cleaning. There were seven cases in which one side was rather worse than the other, either in appearance or itching, with the result that one application might have been at a disadvantage with respect to the other. In these few cases the applications were reversed after a period of seven to eight days and this procedure was of considerable help in deciding which application was the better. It was also found useful in cases where there was discrepancy between the objective appearance of the rash and the sensations as experienced by the patient. Of the 25 cases, 20 were in men and 5 in women. The predominance of men lies in the fact that extensive symmetrical eczema of the limbs in this area is most frequently seen in miners.

Results.

Seven patients did equally well on either application and expressed no preference.

Eleven did equally well on either but expressed a preference for $\frac{1}{4}\%$ prednisolone ointment.

Two did equally well on either but expressed a preference for 1% hydrocortisone ointment.

Two responded poorly to either application.

One obviously did better on $\frac{1}{4}\%$ prednisolone ointment.

Two obviously did better on 1% hydrocortisone ointment.

Summary and Conclusion.

Over a period of four months, 25 cases of symmetrical extensive eczema of the limbs sufficiently severe to require in-patient management were treated with $\frac{1}{4}\%$ prednisolone ointment to the right limbs and 1% hydrocortisone ointment to the left. They were dressed thrice daily by trained nurses. With one exception, the minimum period of treatment was ten days. In the majority of cases, control of the eczema on each side was equally effective by 1% hydro-

cortisone ointment or $\frac{1}{4}\%$ prednisolone ointment. There were only 3 cases out of the 25 which obviously did better on one application than the other. Of these, 2 responded better to 1% hydrocortisone ointment and 1 to $\frac{1}{4}\%$ prednisolone ointment. Where the clinical results were good with both applications, 11 of the 25 expressed a preference for prednisolone ointment, whereas only 2 preferred hydrocortisone ointment. Since the patients did not know which was the newer application and which had been in standard use, it cannot be thought that they preferred the $\frac{1}{4}\%$ prednisolone ointment because they knew it was more up-to-date. The nursing staff who did the dressings were better informed, but they were persistently warned not to suggest any preference to a patient.

It seems that both 1% hydrocortisone ointment and $\frac{1}{4}\%$ prednisolone ointment are effective local remedies and occasional marked preference for one or the other probably arose from the different bases employed.

The hospital bulk price for $\frac{1}{4}\%$ prednisolone ointment is 7s. 6d. for 15 G. That for 15 G. of 1% hydrocortisone ointment is 10s. $10\frac{1}{2}$d. The fact that $\frac{1}{4}\%$ prednisolone ointment is considerably cheaper than 1% hydrocortisone ointment will probably lead to increased use of the former.

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A TRIAL OF TRIMEPRAZINE IN ITCHING DERMATOSES.

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Itching is a common and distressing symptom occurring in many skin disorders where the diagnosis is little in doubt. Some cases of pruritus deserve careful investigation as itching may be the first symptom of serious internal disease, such as diabetes, uraemia, leukaemia and Hodgkin's disease.

To give permanent relief from itching it is necessary to remove its cause. This can be done reasonably easily in such conditions as pediculosis and scabies where the cause is known and is treatable, but in the majority of itching dermatoses the itch-scratch cycle is difficult to break. A drug which would help to do so would be of great benefit in the management of such cases. A new drug, Trimeprazine, has been introduced which is claimed to have antipruritic properties.

Pharmacology.

Trimeprazine is a recently developed phenothiazine derivative which can be regarded pharmacologically as being intermediate between promethazine (Phenergan) and chlorpromazine (Largactil). It is claimed that Trimeprazine has as much or more anti-histamine action as promethazine and also central actions comparable to those of chlorpromazine, but that it is largely devoid of the latter's anti-adrenaline action. In addition it is a powerful spasmolytic. Chemically, Trimeprazine is 10-(3-dimethylamine-2-methyl propyl) phenothiazine, presented as the neutral tartrate.

Method of Trial.

Two separate clinical trials were carried out, one in adults using 10 mg. sugar coated tablets and similar inert tablets as a control, the other in children using a syrup containing 7·2 mg. of Trimeprazine in each fluid drachm without controls.

In adults, many unrelated conditions were included in the trial. After the patient was seen by one of us a secretary who controlled the supply of tablets gave each patient either Trimeprazine or inert tablets and entered the patient's name and the type of table in a book to which only she had access. After a time, usually a fortnight, the patient's pruritus was assessed by any visible decrease in excoriation and by the patient's description of relief or otherwise from itching.

In children, the series consisted of cases of infantile eczema or juvenile atopic dermatitis. The drug was assessed by the diminution or otherwise of scratching and by the parents' impression of improvement or otherwise in irritability or sleeping.

Local treatment, if employed, was that usually prescribed for the condition and in no case was it changed during the time the patient was receiving the tablets.

Dosage in the adult series was usually 10 mg. four times a day, but in a few cases where the pruritus was severe and no drowsy effects were noted this dosage was doubled. In children the dosage ranged from 10·8 mg. to 28·8 mg., in divided doses, according to age, weight and severity of itching.

Results.

Adult series.

The adult series comprised 102 patients and of this total it was subsequently noted from the "key" that 19 patients had received inert tablets and 83 patients Trimeprazine.

Results as calculated from the "key" are shown in Tables I and II.

Table I.—*Change in pruritus in cases receiving Trimeprazine.*

Condition	No. of cases	Marked improvement	Some improvement	No improvement
Atopic dermatitis (Besnier's prurigo)	22	12	9	1
Neurodermatitis	19	13	6	—
Eczema, nummular and stasis	13	2	10	1
Senile pruritus	4	1	2	1
Pruritus vulvae et ani	4	1	2	1
Contact dermatitis	4	1	2	1
Psoriasis	2	1	—	1
Urticaria	1	—	—	1
Prurigo	1	—	1	—
Carbromal eruption	1	1	—	—
Erythroderma	1	—	1	—
Dermatitis herpetiformis	1	1	—	—
Intertrigo	1	—	1	—
Folliculitis decalvans	1	—	1	—
Post-herpetic paraesthesia	1	—	—	1
Lymphatic leukaemia	1	1	—	—
Reticulosis	1	—	1	—
Lichen planus	5	1	4	—
Totals	83	35	40	8

Table II.—*Change in pruritus in cases receiving control tablets.*

Condition	No. of cases	Marked improvement	Some improvement	No improvement
Atopic dermatitis (Besnier's prurigo)	4	—	2	2
Neurodermatitis	7	1	3	3
Eczema, nummular and stasis	5	—	1	4
Pruritus vulvae et ani	2	—	2	—
Psoriasis	3	1	1	1
Urticaria	1	1	—	—
Erythroderma	2	—	—	2
Pruritus in a case of vitiligo	1	—	—	1
Totals	25	3	9	13

Mistakes are difficult to eliminate in any trial and this was no exception. It was found when checking the case notes with the key that four cases whose pruritus had relapsed had by mistake receive a supply of inert tablets after taking the drug for three to four weeks. It was also found that two patients who had started with inert tablets, without relief, had later received the drug with marked relief of pruritus. These six cases appear both in Table I as having improved on the drug and also in Table II as having been on control tablets. They lend support to a favourable assessment of the drug, having been on either Trimeprazine or control tablets unawares and thus acting as perfect controls.

The results were analysed statistically and reported on as follows. "The proportions showing some or a marked improvement were greater in the treated than in the control group. The probability that a consistent advantage of the size obtained, or larger, would have occurred by chance in the trial, if there was no true difference between the effects of the drug and the inert substance, is less than 0·001%, i.e. one in a hundred thousand."

Series in children.

In children the results were as shown in Table III.

TABLE III.—*Change in pruritus* (*all cases received Trimeprazine*).

Condition	No. of cases	Marked improvement	Some improvement	No improvement
Atopic dermatitis or infantile eczema	53	17	31	5

Infants were most difficult to assess, but the great majority of their mothers voiced satisfaction with the syrup. The effect was especially appreciated when during the holiday period the child was without syrup for one or two weeks, and the mothers without exception noticed that the children were more irritable, scratched more and slept less peacefully. Whether relief from pruritus allowed natural sleep or whether the drug had a hypnotic effect is open to argument but the result was the same. Only one parent mentioned that her child was drowsy during the day. In eight cases the mothers noticed no improvement in sleeping; the other forty-five children were noticed to be less irritable during the night.

In both adults and children, trimeprazine would seem to have a place in the relief of pruritus. Table I shows that in atopic dermatitis, eczema and neurodermatitis the drug was beneficial in all but two cases out of a total of fifty-four. This in itself is rather remarkable, especially when one considers the chronicity of most of these conditions. Many of these cases had received antihistamine, sedative and "tranquillising" drugs in the past with only poor effect. The

older patients responded as well as the younger. In the four cases of senile pruritus, three showed improvement. The other conditions listed were not seen in sufficient number to be of much significance, but the drug seems to be a useful adjuvant in the management of any itching dermatosis.

Side Effects.

Drowsiness during the day was experienced by four patients, but this effect wore off, while continuing the drug, after approximately ten days. One woman with lichen simplex, however, complained of slight drowsiness during the whole of a two months' course of the drug.

Swelling of the ankles, lower legs and face was experienced by one patient, who had had a similar sensitivity reaction to chlorpromazine.

Dizziness was complained of by one patient.

Rawness at the tip of the tongue was experienced by one patient but this was probably coincidental, as apart from a haemoglobin of 74%, the blood was normal.

A woman with urticaria complained of severe headaches after taking the tablets for two weeks. She was pleased with the result and had shown a marked improvement. The tablets were stopped and two days later the headaches had ceased. It was subsequently found that she had been on inert tablets. This merely demonstrates the difficulty of assessing any antipruritic drug as the emotional overlay in many of these cases is a decisive factor in the symptomatology.

Liver damage has been reported in patients receiving chlorpromazine and Myers *et al.* (1957) discussed the production of jaundice in their patients who had raised levels of serum alkaline phosphatase. Chlorpromazine jaundice generally occurs between the twelfth and twenty-first day of medication. Although no patient in this series developed jaundice, it was thought worth while to estimate the alkaline phosphatase in a few cases known to have received the actual drug. This was done after the trial in sixteen patients, adults and children and no abnormal levels were obtained, although three were at the upper limit of normal.

Summary.

A controlled trial in adults of a new antipruritic drug, Trimeprazine, is reported. The drug was more effective than control tablets in relieving itching.

Patients with atopic dermatitis and neurodermatitis responded particularly well.

A syrup containing Trimeprazine was used in an uncontrolled trial in cases of infantile eczema and juvenile atopic dermatitis and helped the majority.

Toxic effects were not troublesome.

The drug has antipruritic properties and deserves further trial.

We are indebted to Dr. A. Lyell for the inclusion of some of his cases in this trial and to Mr. W. Brass of the Department of Statistics, Aberdeen University for his analysis of the results. We also wish to thank Dr. R. Forgan, Medical Adviser, Medical Trials Unit, Messrs May & Baker Ltd., Dagenham, Essex, for the supply of tablets and syrup and for details of the pharmacological studies carried out on the product.

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PORPHYRIA DURING CHLOROQUINE THERAPY.

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In 1954, Linden, Steffen, Newcomer and Chapman described porphyria in a case of chronic discoid lupus erythematosus and attributed it to the administration of chloroquine. Davies and Vander Ploeg described two further cases in 1957; one received chloroquine for chronic discoid lupus erythematosus the other for light sensititivy. The following case report describes the occurrence of porphyria during the administration of chloroquine for subacute disseminate lupus erythematosus.

Case Report.

A woman aged 57 years, of dark complexion, attended the out-patient department of the Manchester and Salford Hospital for Skin Diseases in July 1957 complaining of pain and tenderness of the shoulders and chest, accompanied by weakness, of eighteen months' duration. Six weeks before her attendance, she developed a rash on the dorsum of the fingers and later on the face. In 1935 she attended the dermatological clinic at another hospital with a rash of the hands and forearms, which persisted for about six months A similar attack occured in 1940 and remained for about the same period. No diagnosis or records were available.

Examination.—The upper arms and the back of the neck showed well defined plaques of lupus eruthematosus. The face and fingers presented a bluish-red scaly eruption and there was oedema of the eyelids. General physical examination revealed no abnormality. A diagnosis was made of subacute disseminate lupus erythematosus becoming acute and the patient was admitted to hospital.

Family History.—Mother had " septic rash " of arms and legs at age of 10 years. Died aged 49 years, cause unknown. Father died aged 58 years, cause unknown. The patient married at 23 years of age. Children (date of birth given): 1924. Boy. Died aged 16 days. Jaundice; 1925. Miscarriage; 1926. Boy. Died aged 6 months. Whooping cough; 1927. Miscarriage; 1928. Boy. Died aged 2 years. Diphtheria; 1929. Miscarriage; 1930. Boy. Died age 11 years. Diphtheria; 1932. Girl. Alive and well; 1937. Boy. Alive and well; 1941. Boy. Alive and well.

She worked as a cleaner and waitress at a public house from 1944 to 1956, when the present illness commenced.

Investigations.—Hb. 94%. W.B.C's. 5,800, differential count within normal limits. Platelets plentiful. E.S.R. (Westergren) 54 mm. in first hour. Plasma proteins, total 6·6 g.%, albumin 3·5 g.%, globulin 3·1 g.%, γ-globulin 1·03 g.%, A/G ratio 1·13/1. Urinary creatinine 1·054 g. in 24 hours (normal 1·0–1·8 g.). Urinary creatine nil. W.R. negative, Kahn positive (tested twice). L.E. cells were not detected in peripheral blood.

Skiagram of chest. There was an opacity in the right mid-zone posteriorly, which suggested either an effusion or fibrosis in the interlobar septum.

Progress.—She had a persistent low pyrexia (99–100°F.).

Treatment.—Chlortetracycline hydrochloride 250 mg. was given by mouth 6 hourly for 5 days. The pyrexia settled and on the tenth day after admission treatment was

commenced with chloroquine phosphate 250 mg. twice daily. After two days, the patient complained of discomfort in the right renal angle and lower abdomen and her urine became the colour of burgundy wine. Her temperature was 104° F. Chloroquine was discontinued at once and the temperature fell to normal in thirty-six hours. The abdominal pain disappeared and the urine returned to its normal colour. The urine passed during the episode was of specific gravity 1022 and acid reaction ; no albumen and no sugar was present. Ehrlich's aldehyde reagent gave a negative reaction, but under Wood's light a definite red-brown fluorescence could be detected and this increased during the following twenty-four hours. Unfortunately, facilities for estimation of porphyrins were not available at this time. In view of the possible association between porphyria and hepatic damage (Brunsting and Mason, 1949 ; Canivet and Rimington, 1953) and the patient's opportunity for sustaining such damage, liver function tests were carried out a month after admission and showed thymol turbidity 11·2 units %, colloidal gold positive, bilirubin 0·66 mg.% and alkaline phosphatase 13·0 units %.

All clinical signs of porphyria disappeared and the acute phase of the lupus erythematosus went into spontaneous remission. She was discharged with quiescent subacute disseminate lupus erythematosus about one month after admission. In view of the contradictory results of the serological examination, the help of the Venereal Disease Reference Laboratory was sought and Dr. I. N. Orpwood Price reported that he could find no serological evidence of syphilis.

First Readmission.—Four months later, the patient was readmitted as an emergency complaining of cough and severe pain in the right lower chest. The lupus erythematosus was still quiescent, but there was dullness to percussion at the right base with diminished breath sounds and moist sounds. Temperature 101° F., pulse 120 per min., respiration 42 per min. A diagnosis of lobar pneumonia was made and she was treated with chlortetracycline hydrochloride, 250 mg. 6 hourly for 5 days. Her temperature settled slowly over the next twelve days and remained normal for one week, after which an intermittent pyrexia (99–101° F.) developed.

Whilst she was in hospital the opportunity was taken of estimating her porphyrin excretion. Urine (24 hours) : 2·1 litres containing 967 μg. total porphyrins (normal 0–100 μg., Rimington, 1952). Faeces (24 hours) : 354 g. containing 26·8 mg. total porphyrins (normal 200–300 μg., Rimington, 1952).

She was transferred to a general hospital about seven weeks after admission for investigation of her chest condition as skiagrams still showed consolidation at the right base. Three specimens of sputum showed no tubercle bacilli and the E.S.R. (Westergren) was 90 mm. in first hour. In spite of the absence of L.E. cells on repeated examination, it was considered that her pulmonary signs were due to disseminated lupus erythematosus and following treatment with prednisolone by mouth she returned to a quiescent state of subacute disseminate lupus erythematosus. Histological examination of the skin lesion on the neck was carried out at this time

The section showed a rather atrophic epidermis with loss of papillae and slight hyperkeratosis. There were a few small areas of liquefaction degeneration involving the basal layer. Three hair follicles were present and one of these was filled with a horny plug. The dermis showed vascular dilatation and some degeneration of the collagen. There was a minor degree of cellular infiltration which consisted mainly of lymphocytes with a few histiocytes. The appearances were consistent with a diagnosis of lupus erythematosus.

Second Readmission.—About eleven months after readmission the patient was again admitted to the Manchester and Salford Hospital for Skin Diseases with acute dissemination of the lupus erythematosus. Peripheral blood was examined and showed large numbers of L.E. cells for the first time.

She complained of scalding and frequency of micturition, and culture of a catheter speciment of urine produced a growth of *B. coli* sensitive only to chloramphenicol. She received this drug, 250 mg. 6 hourly for 5 days, following which her symptoms

subsided and the lupus erythematosus returned to the quiescent subacute state. She was discharged six weeks later.

It was noticed that since her first attendance in July 1957, the patient's skin had become appreciably darker in colour, particularly in the exposed areas, so that her complexion now suggested that of the Romany people (Brunsting *et al.*, 1951).

Discussion.

A small increase in the excretion of porphyrins is found in porphyrinuria which is not a primary disturbance of porphyrin metabolism and occurs in a variety of diseases (Gray, 1956; Rimington, 1952). Major disturbance of porphyrin metabolism with great increase in porphyrin excretion occurs in the porphyrias. Three clinical types are recognised (Gray, 1956).

(i) Congenital or photosensitive.
Porphyria erythropoetica (Watson, 1954).
(ii) Acute or acute intermittent.
(iii) Chronic or mixed.
Porphyria cutanea tarda (Rimington, 1952).

These are usually regarded as distinct diseases, but may not be so. Watson (1954) regards the acute intermittent and cutanea tarda types, together with the mixed and latent as subdivisions of a single group—porphyria hepatica.

The presence of hepatic damage suggests that the present case should be classified as one of chronic porphyria (porphyria cutanea tarda) and the great increase in porphyrin excretion in the faeces during a period of remission confirms this (Rimington 1952). Davies and Vander Ploeg thought their first case represented a mixed type of hepatic porphyria, but described their second case as porphyria cutanea tarda. Both cases gave a history of heavy consumption of alcohol and investigations confirmed the presence of liver damage. The case of Linden *et al.* showed no evidence of liver damage and the authors thought it should be classified as an acute porphyria in view of the systemic symptoms and early remission. However there was no excretion of porphobilinogen and Rimington (1958) considers this necessary for such a diagnosis. The abdominal symptoms which are so marked in acute porphyria may also occur during the intermittent attacks of porphyria cutanea tarda.

There seems general agreement that the development of porphyria depends on an inborn error of metabolism (Garrod, 1923; Watson, 1951). Recently, Waldenström (1957) has suggested that cases of porphyria could arise as a result of chronic alcoholism and believes them to resemble closely the cutanea tarda type. Gray (1956) states that cases of porphyria cutanea tarda in chronic alcoholics may show no clinical or biochemical evidence of liver disease.

The onset of porphyria so soon after commencing chloroquine therapy suggests a direct toxic action of the drug. London (1957) treated a case of porphyria cutanea tarda with chloroquine, with relief of light sensitivity, but no untoward

symptoms. This suggests that the toxic action of chloroquine is not simply hepatic blockage, preventing the excretion of porphyrins in the faeces, with a consequent rise in the plasma level and overflow into the urine.

Unfortunately the aetiology of the porphyrias is not completely understood and the biochemical errors in chronic porphyria are unknown. In the light of present knowledge, the method of production of porphyria during chloroquine therapy cannot be suggested.

Summary.

A case is described in which porphyria developed after the administration of chloroquine for subacute disseminate lupus erythematosus.

The type of porphyria and its method of production are discussed.

I wish to thank Dr. J. E. Kench, Senior Lecturer in Chemical Pathology at the University of Manchester, for the estimation of porphyrins, and Dr. J. G. Coburn for permission to publish this case.

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ARTERIAL THROMBOSIS APPARENTLY DUE TO STEROID TREATMENT.

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The complications caused by steroid therapy are well known but few cases of peripheral arterial thrombosis have been described. The following report describes two patients who received cortisone treatment for pemphigus and both of whom developed arterial thrombosis.

Case Reports.

Case 1.—A man aged 48. Born in Turkey, he came nine years ago to Israel ; the father of five healthy children and a mason by trade. Four months prior to admission, skin changes appeared on his face, head and chest. Examination in hospital showed a well nourished man in good general condition. The laboratory findings were within normal limits. The clinical diagnosis of pemphigus was confirmed by histological examination of the skin. He was treated with steroids with good results. He received 220 units of ACTH and 6 G. of cortisone in daily doses of 75–400 mg. over 65 days. He was discharged very much improved, with a daily maintenance dose of 75 mg. of cortisone. In 1957 he was readmitted twice because of relapses. On each occasion he improved with augmented doses of steroids.

The steroid treatment caused no complications other than some nervous tension. The patient left hospital in good condition, which enabled him to continue his fairly hard physical work. He was advised to visit the outpatient clinic periodically. He did not follow our instructions and consequently did not receive any further treatment until he had to be readmitted to hospital with a relapse. Typical lesions of pemphigus had developed all over his body ; some were secondarily infected. This time his general and nutritional condition was very poor. E.S.R. 53 mm. in 1 hr., (Westergren), W.B.C. 16,000 per cu mm., differential count and all other laboratory findings within normal limits. We decided on treatment with cortisone 800 mg. daily, decreasing gradually as the patient's condition improved. After 10 days of this treatment, the patient began to complain of severe pains in the right axillary region radiating to the fingers, accompanied by cyanosis of the fourth and fifth fingers. A few days later, there was loss of sensation on the palmar side of his right hand, the radial pulse could not be felt and the ulnar pulse was considerably decreased. Neurological examination showed no abnormal findings. The cyanosis of the fourth and fifth fingers increased, especially of the latter, followed by necrosis of the tip. The patient suffered severe pain. Suspecting a blockage in the brachial artery of his right arm, oscillometry was performed and this showed a definite abnormality.

The patient was transferred to the department of vascular surgery for arteriography. A distinct obstruction was found in the bifurcation of the right brachial artery extending to the middle portion of the radial artery. A recent thrombus 8 cm. in length was removed surgically from the artery. Because of the necrosis, the two distal phalanges of the fifth finger had to be amputated. After the operation, the pain disappeared and the patient returned to our department for further treatment. His general and skin condition was improved gradually by further treatment with

steroids accompanied by anticoagulants. He was discharged from hospital in good condition and is still under observation with a daily maintenance dose of 15 mg. of prednisone.

Case 2.—A woman aged 78. Born in Turkey, she came 8 years ago to Israel ; the mother of two healthy children. Two months prior to admission to hospital, vesicular lesions appeared all over her body. Her general state of health was poor. A systolic murmur was audible over the apex of the heart and the mitral area, B.P.140/70. She had typical pemphigus.

Hb 11·4 g. %, W.B.C. 14,000 per cu. mm., differential count normal, E.S.R. 48 mm. in 1 hr., (Westergren), platelets 160,000 per cu. mm., bleeding and clotting times normal. Because of her severe skin condition, steroid treatment was started with a daily dose of 300 mg. of cortisone ; however, we had to increase the dose to 700 mg. daily before improvement was noted. No complications were observed except for some mental tension. This forced us to decrease the dose of cortisone and then to replace it by small doses of prednisone.

Three weeks later, the patient began to complain of severe pain in her left foot. Twenty-four hours after the onset of pain, the foot became swollen, cold and cyanotic. Arterial pulsation in her left lower limb was absent and only a weak femoral pulse could be palpated. On suspicion of a stoppage in the femoral artery, she was immediately transferred to the surgical department for arteriography and surgical intervention. A fresh thrombus of 4 cm. length was removed from the bifurcation of the superficial femoral artery. Postoperatively, she showed a decreased blood supply to the left leg and soon dry gangrene developed which required a second surgical intervention. The leg had to be amputated above the knee. A recent thrombus in the femoral artery and arteriosclerosis of the amputated leg were found by the pathologist. Since the patient's condition improved satisfactorily, she returned to our department for further treatment with steroids accompanied by anticoagulants. She was discharged from hospital in good condition, with a daily maintenance dose of 100 mg. of cortisone.

Summary and Conclusions.

In two cases of pemphigus treated with cortisone, arterial thrombosis was observed. The thrombosis occurred in the brachial artery in the first case and in the superficial femoral artery in the second. The question arises as to whether the arterial thrombosis was due to the steroid therapy. Because of the histological findings of arteriosclerosis in the second case, it may be suggested that the thrombus was due to arteriosclerosis. In view of the character of the thrombus, which was recent, we consider that the cortisone was a contributing factor in the acceleration of the arterial occlusion. The situation is different in the first case where the patient was relatively young and fit. Except for pemphigus, he had never suffered from any disease and had no signs of arteriosclerosis. No abnormal signs were found in his heart and internal organs. In this case, one must consider the cortisone as the probable causative factor in the development of the thrombus in the brachial artery.

In recent years, many publications have dealt with vascular complications probably caused by cortisone therapy but only a few observations have been published on the increased coagulability of the blood caused by this drug. In 1950, Grossgriff, Diefenbach and Vogt described a series of 175 patients who had received cortisone for various diseases. Eleven thrombo-embolic episodes,

including two cases of fatal pulmonary embolism, were observed. Changes were found in the venous clotting time and heparin-retarded venous clotting time which indicated that steroids frequently produced a hypercoagulable state of the blood. However, in our patients no such blood changes were discovered.

In the light of the facts mentioned above, perhaps it would be advisable to give anticoagulants in clinical situations demanding high doses of cortisone or to patients who are suspected of a predisposition to thrombo-embolism, if they require steroid therapy.

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ROYAL SOCIETY OF MEDICINE.

SECTION OF DERMATOLOGY.

President.—Dr. John T. Ingram.

16 October 1958.

Naevus Lipomatosus Subepidermalis.—Dr. Stanley R. Wood.

A schoolboy, aged 17.

History.—The lesion on the left thigh began to appear about the age of 10 and has gradually increased in area by extending slowly downward, the early appearances around and below the knee being the most recent. His general health is excellent, and there is no family history of developmental anomalies.

Clinical Findings.—On the outer side of the left thigh there is an extensive plaque of discrete and confluent creamy-yellow irregular hemispherical nodules. In places the pilo-sebaceous follicles are prominent and bear strong dark hairs. An earlier stage can be seen in the most recently involved area on the outer side of the knee and upper calf.

Biopsy.—The epidermis shows hyperkeratosis and follicular plugging, but is otherwise normal. In the upper dermis are isolated small groups of fat cells surrounded by a round-cell infiltrate ; in the mid and lower dermis the collagen is fragmented and here and there replaced by large irregular islands of fat cells.

Comment.—This is a rare congenital anomaly of comparatively late onset which since it appears to be an abnormal mixture of normal tissue elements can be pathologically classified as a hamartoma.

Only about a dozen cases have been reported since 1885 when Hyde described what he called " Congenital Naevus Lipomatodes ". Kromayer (1896) described the histological picture and Robinson and Ellis (1937) published the first case with biopsy findings in the English literature.

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Discussion.

Dr. Louis Forman : The degree of connective tissue thickening is definite histologically. This must be a variety of connective tissue naevus.

The President : I thought there was ectopic fat histologically.

Dr. H. Haber : The condition is a clinical and histological entity. The fat is heterotopic in position. It originates from the perivascular reticulum.

Dr. S. R. Wood : Kromayer and the German histologists commented on the collagen ; they think the fat might have arisen as a degenerative process, but Dr. Haber assures me that that cannot be so.

Bullous Pemphigoid and Psoriasis.—Dr. J. Everall (for Dr. G. B. Mitchell-Heggs.

A man, aged 50.

History.—Persistent psoriasis for thirty years. 5 July 1958 (six weeks before admission) was given a course of Ledercort (16 mg. daily, reduced to 4 mg. over six

weeks). During the fifth week developed an irritating vesicular eruption about the hand and feet, becoming generalized after 48 hours.

Previous illness.—Cholecystectomy 1950 ; Diveritulitis 1956.

Family history.—One daughter has psoriasis.

Examination on admission.—Profuse and widespread bullous vesicular eruption on trunk and limbs, a few lesions in mouth. Small plaques of psoriasis splashed about waistband area and extensor aspect of limbs. Some bullous lesions situated on psoriasis. General examination negative.

Investigations.—Skiagram of chest negative. Blood count normal. W.B.C. 10,000 (normal differential). E.S.R. 4 mm./1st. hr.

Histology.—A subepidermal bulla. No acantholytic cells but many eosinophils in bullous fluid.

Prednisone (50 mg. daily) and Ledercort (12 mg. daily) failed to control the eruption but on ACTH gel 20 units b.d. the lesions gradually improved and eventually resolved.

10 September : Prednisone was stopped and ACTH gel was reduced to 5 units, b.d. The electrolytes and the urinary 17-keto and 17-ketogenic steroid output remained normal while under steroid therapy.

Discussion.

Dr. G. B. Mitchell-Heggs : We tried to control the blisters with sulphapyridine also. The question is how long it will be practicable to carry on ACTH injections. A similar case had improved after ACTH, then relapsed but improved on cortisone. This patient's history is the reverse. I shall be interested to hear if any member has had a similar case.

Dr. C. H. Whittle : I think, Mr. President, you are more aware than I of the way that psoriasis can run to bullae or pustules, without provocation from drugs, and become generalized. I am not sure of the time relationship in this patient to the treatment with Ledercort. One does see cases of psoriasis that produce bullae without any apparent specific factor. I believe you saw my patient at Cambridge recently with a generalized pustular phase which might have been provoked by mercury inunction ; but I think psoriasis can spontaneously develop bullae.

Dr. E. Waddington : A patient of mine with pustular psoriasis of the soles was treated with Ledercort. Gradual withdrawal of the drug produced a severe relapse with pustules on the feet and legs, some of which coalesced to form purulent bullae. It seems possible that this is a similar reaction to steroid therapy.

Dr. T. B. Fitzpatrick : Triamcinolone was at first thought to be almost specific in its effect on psoriasis, and indeed the results are perhaps better than those of any previous oral medication. It is doubtful whether the same effects could not be achieved with higher doses of hydrocortisone, and the dramatic responses of psoriasis to Triamcinolone may simply be related to its more potent anti-inflammatory action. I have had two rather harrowing experiences with Triamcinolone in which the psoriasis was transformed from a tolerable nuisance to an exfoliative psoriasis—a medical emergency. Fortunately both patients recovered after several weeks. I do not believe that this patient's present problem is related to his psoriasis.

Dr. G. C. Wells : I saw the patient when the bullous eruption was possibly at its worst when some of the bullae were becoming haemorrhagic and the psoriasis under control. I thought that possibly this was a pemphigoid rather than a peculiar psoriatic expression.

The President : There are three possibilities here, namely that the condition is a variant of pustular psoriasis, or that it is psoriasis and pemphigoid, or that it is a steroid reaction in psoriasis.

I think this is a variant of pustular psoriasis. Members will remember Dr. Barber showing cases of psoriasis with impetigo herpetiformis pattern of reaction superimposed. I have one such patient who in his early days had an eruption of clear blisters from time to time associated with the psoriasis.

Ichthyosiform Erythroderma (Brocq).—Dr. W. Frain-Bell (for Dr. G. B. Mitchell-Heggs).

A farmer, aged 30. South African.

History.—This patient's skin was first noticed to be abnormal about the age of 3 months. The distribution of the abnormality was similar to those now present but to a lesser degree. As far as is known there was no erythematous phase. Blister formation began in early childhood, occurs all the year round but especially during the hot season in South Africa. The blisters occurred particularly at sites of friction but have also appeared on all affected parts at one time or other but never on the

normal skin. During the last 10 years there has been a progressive reduction in blister formation, and although it is now a rare occurrence, small blisters still develop at sites of excessive friction. The abnormal skin changes have otherwise shown little improvement with the passage of time.

Family history.—Both parent are alive and well and are not blood relations. One sister died of pneumonia in infancy but two other sisters and one brother are alive and well. There is no family history of skin disease or other developmental abnormalities.

Past history.—Malaria.

Fig. 1.

Clinical findings.—Abnormal changes are present in the skin over extensive areas of the trunk and limbs. There is a combination of ichthyosis with verrucous hyperkeratosis, particularly so in the limb and body flexures (groins, axillae, cubital and popliteal spaces) Fig. 1. On the limbs the hyperkeratosis is linear in some areas. The hair, teeth and nails are normal.

Histology.—The epidermis shows much hyperkeratosis followed abruptly by an increased stratum granulosum that shows disarrangement and irregularity of keratohyaline granules. The stratum spinulosum which follows also shows a peculiar degeneration with loss of prickles leading to the formation of a "spongiotic" state of the epidermis.

Diagnosis: Ichthyosiform Erythoderma. (Dr. Henry Haber.)

Comment.—The point we wish to make is that ichthyosiform erythroderma varies from case to case and in its development in time. At one extreme there may be hyperkeratotic and ichthyotic patches, differing only in their flexural distribution

and histological changes from simple ichthyosis and at the other extreme the full picture of erythroderma, hyperkeratosis and extensive bullous formation. Between these two extremes there may be many variations. Dr. H. Haber drew attention to the specific acantholytic disintegration of the epidermis shown in the bullous lesion and also from affected skin with no bullae.

Reference.

Wilson, H. T. H. and Haber, H. (1957) *Brit. J. Derm.*, **69**, 329.

Discussion.

The President : I thought it might be porokeratosis. I suppose that is out of the question histologically although the areas Dr. Haber emphasized were in relation to sweat glands.

Dr. G. Hodgson : Arising out of an article in the *Acta Dermato-Venereologica*, **38**, 1958, pp. 51–68. on " The treatment with vitamin B_{12} in Ichtyosiform Erythroderma ", by A. Lodin, H. Gentele and B. Lagerholm, we treated the patient with gross ichthyosiform erythroderma (Brocq) who was shown at Cardiff. He is still under treatment. Initial doses of 1000 micrograms were given daily and he is now after some weeks of treatment receiving 6000 micrograms daily. There has been considerable improvement. The large conical projections which he exhibited can now be detached and separate off quite easily, which they did not do before. It is a little early to say what will be the end result of this therapy.

Dr. H. Haber : In porokeratosis Mibelli the epidermis shows acanthosis and atrophy with a nonspecific inflammatory reaction in the cutis. As such the histology is not diagnostic. The only typical feature is the presence of parakeratotic columns in the stratum corneum. These columns can sometimes be seen arising in sweat pores which when present give the histological picture a characteristic and diagnostic appearance.

The histology of the bullous type of ichthyosiform erythroderma and a certain type of ichthyosis hystrix is typical. There is marked hyperkeratosis and also acanthosis. The typical feature is the presence of a marked disintegration of the granular layer. The cells are indistinct, degenerated, the keratohyalin " spilled ". The stratum spinulosum shows a peculiar degeneration of the cytoplasm of individual prickle cells, similar to the changes seen in epidermodysplasia verruciformis of Lutz and Lewandowsky. The changes in the prickle cell layer lead to an " acantolytic " process producing cracks within it. Fluid from the underlying corium accumulates to produce intra-epidermal vesicles.

The following cases have been published in *Proc. R. Soc. Med.* **52**, 189.

Behçet's Syndrome.—Dr. Brian Russell.

Cutaneous Arterioliti swith Splenomegaly.—Dr. Buchanan (for Dr. S. C. Gold).

Auriculotemporal Syndrome.—Dr. M. Feiwel.

The following cases were also shown :

Multiple Skin Necrosis (Arteriolar).—Dr. J. Savage.

Pigmented Lichenoid Eruption of Calves following Prolonged Hypostasis.—Dr. Brian Russell.

Dermatomyositis and Carcinoma of Breast.—Dr. Brian Russell.

Darier's Disease.—Dr. J. S. Pegum.

Epidermolysis Bullosa Dystrophica.—Dr. M. Ridley.

Primary Tuberculous Complex of Skin.—Dr. M. J. Coggin (for Mr. M. Harmer and Dr. M. Feiwel.)

Case for Diagnosis, ? Lichen Planus, ? Leucoplakia.—Dr. M. Feiwel.

Case for Diagnosis, ? Lichen Nitidus.—Dr. W. Frain-Bell (for Dr. Brain).

NORTH OF ENGLAND DERMATOLOGICAL SOCIETY.

Nottingham, October, 1958

Primary Self Healing Squamous Cell Carcinoma (Ferguson-Smith).—Dr. D. I. McCallum.

Housewife. Aged 51 years. Twenty years ago the patient's first lesion, which she relates to the birth of her son some months previously, developed on her left forearm. Since that time she had developed new lesions, frequently several per year. They run a course of varying duration and ultimately heal leaving depressed scars that affect the face, forearms, left hand, buttocks, vulva, knees, legs and ankles. Pain has been a feature of many of these lesions, especially those on the vulva, legs and ankles.

Histopathology.—Well differentiated keratinising squamous cell carcinoma.

Treatment.—Treatment has included radiotherapy to the nose, left leg and vulva, and excision of lesions on left forearm and right thigh. With considerable experience of the natural history of the condition, the patient is in no doubt that she wishes to leave new tumours to heal spontaneously.

There is no family history of the condition. There is no history of bromide or iodide administration.

Present Condition.—Button type carcinomata are at present visible on the left elbow and on the left side of the upper lip. According to the patient these will have healed with scarring in a year.

Calcinosis Circumscripta.—Dr. D. I. McCallum.

Male aged 34 years. Light brown plaque 2 in. by 1 in. over sacro-coccygeal region on which numerous light coloured, hard nodules were apparent. The patient has been aware of these nodules from the age of nine, and he is of the opinion that they have extended very gradually since then.

Biopsy Report.—" Section shows the dermis to contain coalescing areas of amorphous or granular calcium deposits, around which, in places, there is a scanty foreign body giant cell reaction. The appearances are those of (idiopathic) calcinosis cutis."

Biochemical Findings.—Serum calcium, 10·2 mg. per 100 ml. Acid phosphatase 0·5 units per 100 ml., Alkaline phosphatase, 4 units per 100 ml. Serum cholesterol, 180 mg. per 100 ml.

No history of antecedent trauma, and no relevant family history. No evidence of spina bifida, nor of pilonidal sinus. There are no subjective phenomena, but on occasion a lesion has discharged a " white cheesy material ".

Sarcoid.—Dr. P. D. C. Kinmont.

Housewife, aged 62. No contact with beryllium. Pneumonia 1955. Influenza October 1957. Referred to E.N.T. Department in April 1958 with dryness of the mouth and eyes since March. Bilateral parotid swelling with aching first appeared in January. She developed burning patches on the back in mid April. Apart from aspirin, she had had no drugs before the eruption appeared.

Examination.—Bilateral parotid swelling. No lymphadenopathy. No uveitis. Chest and heart N.A.D. No hepatomegaly or splenomagaly. There were numerous infiltrated nummular patches of erythema with brown punctae and slight scaling on the trunk, arms and right shin.

Progress.—Had an attack of severe pain in the epigastrium and under the left costal margin in June which persisted for a week. She complained of malaise, anorexia, loss of weight, dyspnoea on exertion, orthopnoea and swelling of ankles towards the end of the day.

She developed enlarged sub-mandibular glands in August and two subcutaneous nodules at the Mantoux site and right sterno-clavicular joint. More plaques appeared and she had sheets of erythema between the knees and ankles. She could only take fluids and her vision was deteriorating. In September the infiltrated plaques started to subside leaving pigmentation.

Investigations.—W.R. doubtful +, flocculation +, haemoglobin 104 Red blood cells 5,36. Total leucocytes 3,800. Eosinophil polymorphs, 1%. Neutrophil polymorphs, 56%. Lymphocytes, 43%. E.S.R., 12 mm.

9.vii.58.—Skiagrams: chest normal. Hands normal apart from slight carpal and wrist osteoarthritic changes.

Serum proteins 7·1, Normal A/G ratio. Urine normal.

Biopsy—" Focal collections of epithelioid cells are scattered throughout the dermis. One or two multi-nucleated giant cells of Langhans type are present; no necrosis is seen. There is little or no small round cell infiltration but an occasional polymorph is present. The overlying epidermis is thin. No acid-alcohol-fast bacilli are seen. The appearances are those of a granulomatous reaction which may be due to tuberculous infection or sarcoid.

1.viii.58.—Serum calcium 10·4 mg./100 ml.

7.viii.58.—Mantoux 1 : 1,000 negative.

Treatment.—Local—Quotane, Eurax. To the mouth—Sat. Soda Bic. 75 : Glycerine 25.

" Congenital " Erythematous Macular Eruption. A Case for Diagnosis. —Dr. I. Anderson.

A girl aged 6.

History.—The eruption was first noticed a few hours after birth and she has never been completely free from it since apart from a few days when she had measles at the age of two. She was first seen at the age of six months and on many occasions since, and the lesions are always as at present. They can appear on any part of the body, persist for about twenty-four hours, then fade and are replaced by others. There is practically no itching. The eruption is not influenced by rest in a hospital bed, antihistamines, or oral Prednisolone.

Two years ago she developed arthritis of the right knee which was thought to be a tuberculous infection. However, after four months treatment with Streptomycin the arthritis appeared also in the left knee and a diagnosis of rheumatoid arthritis was made.

Examination.—The eruption which is scattered over the face, trunk and limbs consists of bright erythematous macular lesions one to two centimetres in diameter. Here and there is a tendency to ring formation.

Investigations.—Electrophoresis of serum, normal protein pattern. Blood W.R. and Kahn negative. Skiagram of chest normal. Blood count, microcytic anaemia —haemoglobin 65%—W.B.C. 14,000.

Postscript.—4th March 1959.

In the discussion of this case it was suggested that the eruption was similar to that seen in Still's disease. The patient was subsequently admitted under the care of Dr. E. G. L. Bywaters at Taplow, and his opinion is that this is the condition described by Isdale and Bywaters (1956). There are, however, some extraordinary features and the child is still under observation and investigation.

Reference.

Isdale, I. C. and Bywaters, E. G. L. (1956) *Quart. J. Med.*, 25 37.7.

Chronic Granuloma. A Case for Diagnosis.—Dr. I. Anderson.

A man aged 70. Retired.

History.—Two and a half years ago this patient noticed a nodule developing in the skin of the right thigh. Gradually new lesions appeared on his chest wall and upper arms. They did not itch. During the last few months several of the larger lesions have ulcerated. His skin has been dry since birth.

Examination.—The skin of the chest wall, abdomen, upper thighs and upper arms is infiltrated with brownish red papules and nodules. There is superficial ulceration of several large nodules on the back and in other places there is atrophy of the centre of the lesions with a sclerodermatous appearance. He has some enlarge lymph glands in the neck and axillae, but the spleen is not palpable.

Investigation.—Biopsy of two areas showed an identical histological picture : " In the superficial corium there is a dense inflammatory exudate mainly of lymphocytes and fibroblasts with large numbers of Langhans giant cells."

Blood W.R., Kahn, P.P.R. and T.W.R. negative. Urine : albumin +, sugar +, granular casts present. Mantoux, 1 : 100 negative. Blood sugar curve 122 mg. % rising to 230 mg. % after one hour. Skiagram of chest normal.

Postscript. Male Age 70. 4th March 1959.

This patient died of bronchopneumonia in February 1959. The essential features of skin histology at post mortem were gross collagen degeneration of the mid corium with inflammatory exudate of the superficial corium and foreign body granuloma formation. The lesion extended into underlying muscle which showed a marked myosotis. Deep tissue such as spleen, pancreas, adrenals and lymph nodes showed a pleomorphic cellular infiltrate with the formation of foreign body granuloma. There were hypertensive changes in the kidneys, with some glomeruli suggesting the " wire loop " appearance of L.E.

ANNOUNCEMENT.

INTERNATIONAL COMMITTEE OF DERMATOLOGY.

Meeting of the 27th of October 1958—Paris.

Present :

Dr. Marion B. Sulzberger, President ; Dr. Sven Hellerström, Secretary General ; Dr. R. Degos ; Dr. F. Flarer ; Dr. J. Gay Prieto ; Dr. W. Jadassohn ; Dr. F. Kogoj ; Dr. S. Lapière ; Dr. A. Marchionini ; Dr. G. B. Mitchell-Heggs.

Absent and Excused :

Dr. L. Brunsting, Dr. C. H. Flodén and Dr. M. I. Quiroga.

1. Reports of Drs. Gay Prieto and Hellerström concerning the steps which have been taken to have our League named a " nongovernmental " member of the W.H.O. M. Bertrand of the W.H.O. let us know that our request will be considered in January 1959.

Dr. Gay Prieto believes that if our request is accepted, it would be advantageous to have a permanent delegate of our Committee to remain in close relation with the W.H.O.

Upon the motion of Dr. Degos, Dr. Jadassohn was unanimously appointed to be our permanent delegate.

2. Report of Dr. Degos on the C.I.O.M.S. to which he had been named representative of our League of Dermatological Societies. The question to be considered is that of whether we should take steps to become titular member instead of associate member of this organization.

The Committee unanimously decided to maintain our present position as associate member, but stated that the question of changing this membership could be discussed again at the next meeting of the International Committee of Dermatology.

3. It was decided that the next meeting (the official meeting) of the International Committee of Dermatology would take place in September 1960 in Geneva, Switzerland.

4. The XIIth International Congress of Dermatology will take place in Washington, from the 9th to 15th of September 1962. The president will be Dr. M. Pillsbury, and secretary Dr. E. D. Osborne.

5. Dr. Sulzberger reported on the steps which have been taken in the United States in approaching the government and various organizations for financial support of the next International Congress of Dermatology.

6. The American organizers of the Congress, that is, the Committee for the XIIth International Congress, hope to be able to obtain a certain number of travel stipends which could be distributed to young dermatologists in order to enable them to come to attend the International Congress.

It was moved that the Secretary of the Congress, Dr. Osborne, be requested to secure from Dr. Hellerström, the names of the delegates of each country so that he, Dr. Osborne, could request that these delegates suggest the names of scientists who they think merit assignment of travel stipends to help them attend the Congress. The actual distribution of the stipends will be the prerogative of the Committee of the XIIth Congress.

7. The International Committee decided that the national delegates for the next Congress should be named before the next meeting of the International Committee of Dermatology, that is, before July 1960.

Dr. Hellerström will take the necessary steps to inform the National Societies so that they will have time to elect their delegates before the next meeting of the International Committee.

The national delegates will also be requested to submit before the next meeting of the International Committee a list of opening discussers who they suggest to participate in the different subjects reported on at the Congress.

8. The International Committee of Dermatology decided that the President and the Secretary General of the next Congress should be invited to the next meeting of the International Committee in Geneva in September 1960 in order to give their opinion concerning the organization of the forthcoming Congress and particularly concerning its scientific programme.

9. In order to assure liaison between the International Committee of Dermatology and the Committee of the XIIth International Congress, it seem indispensable that the President of the International Committee, Dr. Sulzberger, be *ex-officio* member of all principal Committees of the Congress, and in particular, of the scientific Committee.

10. In accordance with paragraph 2 of the statutes of the International League of Dermatological Societies, the scientific programme of the Congress must be established by the International Committee of Dermatology at the time of its meeting in September 1960, insofar as it concerns the choice of subjects as well as that of the speakers.

11. The Committee accepts the proposition of Dr. Sulzberger and Dr. Hellerström to organize the forthcoming Congress in the following manner :

3 days : reserved for the principal topics, with a suggested minimum of six and in each of the lecture rooms simultaneous translation.
Forenoon : Statements of the official reporters.
Afternoon : Discussion of the reported subjects of the morning, all with simultaneous translation.
1 day : Symposia (10 to 15 taking place at the same time).
1 day : Case presentations.
1 day : Free.

At its forthcoming meeting, the International Committee of Dermatology will choose the principal topics, the speakers, the directors of discussion, those who are invited to open the discussion, and the topics of the symposia.

12. The Presentation of Cases at the Congress : Dr. Sulzberger proposes that in consideration of the very great number of enrollees that are awaited, to show the cases by television.

A Committee restricted to clinicians that are highly qualified (about 40) which will be selected in advance by the International Committee of Dermatology, will be the only ones authorized to see the cases directly, in order to open their discussion before the body of the enrollees of the Congress.

13. The Contribution of the Participating Societies to the International Committee of Dermatology. Dues : The societies which will have paid their dues (for the period of 1957 to 1962) before the next meeting of the International Committee of Dermatology in September 1960 will have the right : (1) to send their delegates to the Congress, (2) to propose the names of individuals who they think deserve the travel stipends, (3) to propose names for opening discussers. The societies which will not have paid their dues by September 1960 will not have any of these rights, unless the Committee believes that they have shown good and sufficient reasons for demanding a delay in payment.

14. The present protocol, edited by Drs. Sulzberger, Hellerström and Degos, will be sent to all the different participating societies.

The Executive Board of the World Health Organization at its twenty-third session January 1959 decided to admit the International League of Dermatological Societies into official relations as a non-governmental organization with the World Health Organization.

BOOK REVIEWS.

Fungous Diseases and their Treatment*.

This is the published version of a Symposium on Medical Mycology held in July 1957 at the Institute of Diseases of the Chest, Brompton Hospital, London, under the aegis of the British Postgraduate Medical Federation, with the financial support of Messrs. Squibb & Sons.

The book opens with a succinct, well-illustrated review by Dr. Riddell of the role of fungi as pathogens, and Professor Symmers follows with some interesting histopathological observations on systemic infections, which are becoming less rare in this country. Professor van Breuseghem summarises very briefly the pathogenesis of tinea infections : and there follow two papers on *Trichophyton rubrum* infection, a condition almost unknown until fifty years ago, but found increasingly frequently in the tropics, and now, probably because of the closer contacts between the tropical and western races in two world wars, well established in Europe and the U.S.A. Its frequency, its diverse clinical features and its intractibility—especially in the nail plates—render it for dermatologists a subject well worth studying : Dr. Calman deals adequately with the clinical features and Miss Mary English with the epidemiology.

The papers are rather arbitrarily divided into two sections, the second being chiefly concerned with therapy. But throughout there runs the perpetual problem of the relative importance—and the fluctuating relationship—of host and parasite. Dr. Holmes touches on it in his review of tinea pedis in miners, Dr. Winner discusses immunity in experimental candida infection, Drs. Bound, Bodian and Cathie are interested in it in infantile moniliasis and Dr. Dawkins in vaginal moniliasis : candida naturally attracts attention because of its saprophyte to parasite phase change. Dr. Barlow, in a thoughtful chapter on the theoretical aspects of treatment of skin infection, shows appreciation of the complexity of the keratin-fungus relation, and the theory he adopts has since been proved partly correct in the successful treatment of nail and hair infection with Griseofulvin given by mouth. Drs. Brian Russell and Beare cover the clinical aspects of treatment of skin infection, while Dr. Stewart in a careful assay evaluates the action *in vitro*, and Dr. Drouhet in clinical trials, of the newer antifungal agents.

Deep mycotic infections are also discussed. Dr. Charlotte Campbell and Dr. Phyllis Edwards have investigated the serological aspects of histoplasmosis, with geographical surveys : and successful treatment with Amphotericin B in some 60 cases of deep mycotic infection is described by Dr. Furcolow. Pulmonary infections are covered by Dr. Hinson and Dr. Segretain (broncho-pulmonary aspergillosis), Dr. Citron and Dr. Pepys (bronchial sensitivity tests), Dr. Fuller (farmer's lung) and Dr. Pierce (radiological aspects).

This collection of papers on differing subjects, seen from widely different angles, would seem at first sight unpromising material for a book : the standards vary, some of the papers describing careful original work, others merely reviewing work already published or known. The editors have managed, probably with vigorous pruning, to reduce their subjects to a semblance of order within two covers. The result has much to commend it. The shape and format, and the quality and quantity of the illustrations make the book pleasant to read and handle, and it should have a good reception amongst the growing number of medical men interested in clinical mycology.

C. H. W.

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* *Fungous Diseases and their Treatment.* Edited by R. W. Riddell and G. T. Stewart (1958). London : Butterworth. Pp. 256, figs. 145. Price £2 5*s*.

Psychotherapeutic Drugs*.

In the preface to this monograph the author comments that the drug-reaction has taken over the role of syphilis as " The Great Imitator ". He goes on to examine a number of so-called tranquilisers and lists a most formidable number of side-effects and toxic reactions which accompany their use. Many of these effects are manifested in the skin. For that reason alone the author's description of these drugs makes the book useful to the practising dermatologist. It would be still more useful had the book included some information about the possible mechanism of these reactions and their relationship to the pharmacology of the drug.

Half of the book is devoted to the phenothiazine group of drugs. The author quotes a number of papers describing the use of these drugs in dermatology and gives details of a number of clinical trials in the field of dermatology conducted by himself and his colleagues. Unfortunately the absence of data about control studies makes it difficult to assess the value of these trials.

Smaller sections are given to descriptions of the rauwolfia alkaloids, meprobamate, benzactyzine, atarax and two drugs, ectylurea and oxanamide, of which your reviewer has no experience. The last of these is singled out by the author as being of greater value and safety than the others described. From this list of drugs it will be seen that the term " Psychotherapeutic Drugs " has to the author only a very limited application. The barbiturates are not discussed except in comparison with meprobamate. Nevertheless, there is a strong body of opinion which considers that the tranquillisers have little to recommend them when compared accurately with the short-acting barbiturates. And the barbiturates, at least, are very much cheaper. The phenothiazine drugs and rauwolfia alkaloids have a proven limited value in the treatment of certain psychoses. But there is not much evidence for their usefulness in relieving tension and anxiety and a great deal of evidence to show that they are potentially dangerous drugs.

As a guide to therapy this book has little to offer and in justice to the author no major claims are made beyond saying that the drugs can be useful adjuncts to normal dermatological treatment. Outside the field of dermatology the author is somewhat uncritical when discussing the list of ailments said to be alleviated by chlorpromazine. To suggest that a potential hepatotoxin is of use in certain cases of acute prophyria and hyperemesis gravidarum seems to be carrying " the hair of the dog that bit you " principle to dangerous lengths.

The author concludes by saying that these drugs are no substitute for accurate diagnosis and treatment and that physicians who prescribe them indiscriminately are at fault rather than the drugs themselves. With this comment most readers will whole-heartedly agree.

F. A. W.

Leprosy.†

The reviewer recalls with pleasure the memory of a fortnight spent in Vellore and Saidapet, Madras Presidency, in the summer of 1943, when he was privileged to listen to the teaching and to observe the practical skill of the Editor of this book. Through his thoughts run a single theme, the impression gained of a physician dedicated to a great task, that of stimulating world wide concern with a disease until then comparatively neglected by clinicians, public health authorities and social workers alike.

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* *Psychotherapeutic Drugs*. Ashton L. Welsh (1958). Springfield, Illinois : Charles C. Thomas. Pp. 139.

† *Leprosy in Theory and Practice*. Ed. R. G. Cochrane (1959). Bristol : Wright. Pp. 424. 189 illus. Price 84*s*.

In this task it is now true to say that Dr. Cochrane has succeeded. Leprology has been put " on the map " in the sense that it has at last become a subject of real challenge and interest to leaders of medical thought, and in this very uphill battle he is one of a comparatively small group of medical men and women who have borne the heat and burden of the day.

The book itself is the combined work of the Editor and of a team of brilliant collaborators which he has gathered around him. In general, the treatment of the subject matter closely follows that of Dr. Cochrane's previous volume published in 1947 with additions, notably the chapter on eye signs in leprosy by Mr. D. P. Choyce and that on the orthopaedic management of deformities by Mr. Paul Brand. Any criticisms which can be levelled at such a beautifully illustrated and comprehensive volume are of minor nature, but include the surprisingly poor quality of reproduction of the black and white photomicrographs illustrating the otherwise excellent section on pathology and the omission of any mention of the use of the more recent anti-histaminics, such as chlorpromazine, in the prophylaxis and management of acute reactional states in leprosy.

These criticisms apart, this is a great book and constitutes a major advance in the history of progress in leprology.

A. G. F.

Hair Hazards.*

This book on accidents which may occur to the hair, scalp and skin is concerned largely with hair dyes, colour rinses and particularly permanent waves of various types which may cause a reaction in susceptible people. The authors have great experience in this particular field and have covered the possibilities from every angle.

The legal implications are considered at great length, and from these the conclusion is reached that every technique of the type mentioned above should be preceded by a patch test which should be read after 48 hours, otherwise the hairdresser is liable to heavy damages should anything go wrong.

The primary irritant nature of the various solutions used is pointed out and the subject of allergic response in the individual is given due recognition.

R. M. B.

Hair.†

This book is composed of a series of papers derived from those presented at the conference on The Biology of Hair Growth held in London in 1957. The problem of hair growth attracts the attention of people working in widely separated fields and these papers are written by anatomists, biochemists, dermatologists and research workers in the wool industry. The methods used to study it include electron microscopy, histochemistry, radioactive isotope techniques and those of experimental biology and biochemistry. The problems of alopecia and pathology have been deliberately excluded ; nevertheless the book is of great interest to the dermatologist, and some of the methods described should be of use to the clinician wishing to study hair in relation to disease ; for example van Scott's technique of plucking out scalp hairs and grading them according to whether they are in the growing or resting phase.

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* *Les Accidents par Produits Capillaires. Étude clinique, expérimentale, médico-légale.* E. Sidi and R. Longueville (1958). Paris : Éditions Flammarion. Pp. 143. Price unstated.

† *The Biology of Hair Growth.* Edited by William Montagna and Richard A. Ellis (1958). London : Academic Books Ltd. Pp. 520. Price £5 7*s* 6*d*.

Hamilton's comparative studies of hair growth in Caucasian and Japanese men and women show that facial hirsutes and scalp baldness are largely genetic and racial. Now that we have a large resident coloured population it should be possible to do similar comparative studies in the United Kingdom. According to Chase, in hereditary-pattern baldness in men, the hair follicles change from a type with a long growing phase and short resting phase to one with a short growing but long resting phase. Ryder discusses the nutritional factors influencing hair and wool growth in sheep and states that although nutrition is important in providing the means whereby a sheep can express its genetic potentialities for wool production, no amount of extra feeding can make it exceed its genetic maximum. This book therefore does not encourage us to believe that at present two hairs can be made to grow where only one grew before, although Billingham describes the phenomenon of hair neogenesis in adult mammals. His account of how new hair follicles arise in the epidermis which covers the raw area left behind by the shedding of the antlers in deer is of great interest. Fitzpatrick, Brunet and Kukita in an admirable survey of hair pigmentation include new material about the yellow pigment (pheomelanin). They and elsewhere in the book, Chase, give explanations of the process of greying in the hair. Montagna, the driving spirit behind this book, writes in the preface and summary as well as contributing to some of the chapters. Like other books of the " symposium " type, this one suffers from a certain indigestibility, the result of cramming so many facts into it, and also the result of being written by experts in different fields using their own technical languages. It would no doubt help if in future works of this kind contributors made definitions of the specialist terms they use which could be put in a glossary at the end of the book. There are many excellent illustrations and numerous references. J. S. P.

CURRENT LITERATURE.

EOSINOPHILIC GRANULOMA OF THE LUNG. H. J. Livingston. (1958) *New Engl. J. Med.*, **259**, 959.

A woman with an eosinophilic granuloma of the lung developed peculiar lesions in the skin. The nature of the skin lesions was not ascertained with certainty. A. D. P.

HEPATITIS AND CIRRHOSIS IN WOMEN WITH POSITIVE CLOT TESTS FOR LUPUS ERYTHEMATOSUS. L. G. Bartholomew, A. B. Hagedorn, J. C. Cain and A. H. Baggenstoss. (1958) *New Engl. J. Med.*, **259**, 947.

A woman with what appeared to be systemic L.E. developed intermittent jaundice and hepatic dysfunction. It is suggested that systemic L.E. may cause liver disease. A. D. P.

THE CLINICAL AND DIAGNOSTIC IMPORTANCE OF UNRECOGNIZED FOCI OF FUNGI. T. Schulz, E. Weiss and M. Oros. (1958) *Ann. Derm. Syph., Paris*, **85**, 420.

The authors believe that many eruptions up to now considered as dysidrotic eczema, tylosis, chronic urticaria, eczematides, miliary impetigo etc. are really "mycides" and capable of rapid cure if the primary focus is eliminated. They support this suggestion by some figures. F. F. H.

HYPODERMIC VASCULAR ALLERGIDES. B. Duperrat and J. Monfort. (1958) *Ann. Derm. Syph., Paris*, **85**, 385.

This comprehensive article divides these conditions into six groups. (1) Epidermo-dermic, which includes Gougerot's nodular allergide. (2) Periarteritis nodosa. (3) Dermo-hypodermic, which are mostly nodular and include nodular vasculitis and Bazin's disease. (4) Erythema nodosum. (5) Thrombophlebitis migrans. (6) Weber-Christian disease. The third group is most fully discussed and findings in twenty-five of the authors' own cases are presented. There is an extensive table comparing the different features of these six conditions. This is a useful summary but contains nothing essentially new. F. F. H.

INVESTIGATIONS INTO THE STERILIZATION OF PATHOGENIC FUNGI BY ULTRA VIOLET IRRADIATION. J. Coudert and J. Rondelet. (1958) *Ann. Derm. Syph., Paris*, **85**, 412.

The law in France demands sterilization of hairdressing equipment and various forms of apparatus have been designed to achieve this by U.V.R. The authors show that they are ineffectual. F. F. H.

FIRST EXPERIMENT WITH THE USE OF "EPILIN" IN THE TREATMENT OF MYCOSES OF THE SCALP. A. M. Arievich and O. V. Tyufilina. (1958) *Vestnik Derm. i Ven. (Moscow)*, **4**, 29.

The authors have named a complex compound of ethers of para-oxy-fatty aromatic and aromatic ketones synthesized at their suggestion "epilin". This preparation they find to be as good or even better than x-rays or thallium acetate for treating fungous infections of the scalp. It is used as a 2% ointment in a lanolin vaseline base (sperm whale oil even better) or more recently as a 4% plaster. In all, 124 children (school, pre-school and crib stage) were treated; and 1 adult (with chronic trichophytosis). One patient had favus, the others, large or small spored ringworm. After clipping or shaving the hair, the ointment is rubbed into the scalp once or twice daily for 6 days in a week (paying particular attention to the diseased area) and covered with gauze or a bandage (without cotton wool). Epilation follows as a rule in 18/20 days from the start of treatment (even as early as 10/12 days in young children, and as late as 30/35 days in some older children). In one, epilation occurred in 20 days, after 5 days inunction. In only 2 was there unsatisfactory epilation. The dosage is according to body weight, e.g. 2–2·5 gm. of 2% epilin ointment or of the 4% plaster in the day for a body weight of 10–14 Kg. A table of dosage is included, also a photograph showing the complete epilation; and one the regrowth of normal hair. The hair bulbs are atrophic on epilation; and the author stresses that epilation is complete over the whole scalp even if one area only is treated. Growth of hair follows usually 6 weeks after epilation but can be as early as one month or as late as 2 or even 2½ months. Epilation is assisted manually

over the diseased area, and during the bald stage, 2% iodine is applied ; and a tar and sulphur ointment.

There were 92% recoveries and 8 relapses ; and the children were kept under very close observation for side effects by means of blood and urine analyses ; attention was paid to the general health. No general side effects were noted. In 30 children a follicular hyperkeratosis appeared at the site of inunction of the epilin ; and a lichenoid eruption which appeared at the time of epilation was probably lichen microporosis. Easily treated conjunctivitis or blepharitis was encountered and also in a considerable number " pyoderma " of the scalp. The authors do not say which type of mycosis was prone to develop " pyoderma ". In all patients (95) observed after 3–12 months the hair had grown in completely and evenly. M. S. S.

THE ASSOCIATION OF PSORIASIS WITH BLOOD GROUPS. G. K. Hargreaves and F. F. Hellier. (1958) *A.M.A. Arch. Derm.*, **78**, 438.

There is no significant association between psoriasis and any particular blood group. Contrary findings may be explained by the fact that controls were not selected from exactly the same material as patients. J. K.

A CRITICAL EVALUATION OF THE EFFECT OF STEROID LOTIONS ON INFLAMMATORY DERMATOSES. Ira Leo Schamberg, Samuel I. Askovitz and Marvin Greenberg. (1958) *A.M.A. Arch. Derm.*, **78**, 490.

The investigation was undertaken by " double-blind paired-comparison studies ". A total of 510 patients suffering from various inflammatory dermatoses were investigated. Of these 177 showed no difference in reaction to 0·1% fludrocortisone lotion and a control lotion ; 217 showed no difference in reaction to 0·1% fludrocortisone and 1% hydrocortisone lotions ; and 116 showed no difference in reaction to 1% hydrocortisone and 1% prednisolone lotions. An attempt is made to explain these findings. J. K.

ATYPICAL FEATURES IN FAMILIAL BENIGN CHRONIC PEMPHIGUS. Thomas W. Lyles, John M. Knox and J. B. Richardson. (1958) *A.M.A. Arch. Derm.*, **78**, 446.

Six cases of familial benign chronic pemphigus are described which showed atypical features making them easily confused with other dermatoses. In one case the lesions in the groins were markedly verrucose ; in the second, which was precipitated by pregnancy, the vulva only was affected ; the third showed unusual distribution in that the hairline was affected as well as the axillae in summer ; the fourth was diagnosed as disseminated neurodermatitis ; the fifth had annular lesions on the back resembling tinea and the sixth resembled monilia infection of the folds. Only two cases had a familial history but histological examination of the lesions made the diagnosis clear in all. J. K.

A CONTRIBUTION TO THE KNOWLEDGE OF THE ALTERATION OF THE PROTEINS AND OF THE GLYCOPROTEIN AND LIPOPROTEIN COMPLEXES IN THE PLASMA OF BURNED PATIENTS. M. Bonelli and G. Armuzzi. (1958) *Giorn. ital. Derm.*, **99**, 291.

The changes in ten patients were proportional to the severity of their burns. Loss of protein affects the albumen and especially the albumen part of glycoprotein. The α-globulin and α-globulin part of glycoprotein are greatly increased and γ-globulin is increased to a lesser degree. A. L.

PSEUDO-PAGET OF THE SCROTUM. G.-K. Steigleder. (1958) *Dermatologica*, **117**, 165.

A detailed clinical and histopathological account of a case closely resembling one recently reported by Miescher as " Morbus Paget with Involvement of the Skin and Sweat-glands with Pigmentation resembling Melanotic Precancerosis ". Steigleder's case was of shorter duration, 3 years as opposed to 8, and showed an earlier stage of the process. In his opinion it is clearly one of precancerous melanosis, and not Paget's disease, and he thinks that Paget of the genital region is much rarer than has been thought, because of this simulation by the melanosis, giving rise to errors in diagnosis. J. F. S.

PATHOLOGICAL CHANGES ASSOCIATED WITH DEODORANT PREPARATIONS CONTAINING SODIUM ZIRCONIUM LACTATE : AN EXPERIMENTAL STUDY. J. T. Prior, Herman Rustad and G. A Cronk. (1958) *J. invest. Derm.*, **30**, 449.

Mainly about the effects of injecting deodorant lotions into the subcutaneous tissues of white rabbits. J. H. T. D.